Letter to the Editor

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In reply re: The relationship between estrogen and subsequent growth restriction among adolescents with heavy menstrual bleeding at menarche

Keywords: menstrual bleeding; growth restriction; estrogen

To the Editor,

We appreciate the critical review shared by Emrullah Arslan and Samim Ozen [1] regarding our article “The relationship between estrogen and subsequent growth restriction among adolescents with heavy menstrual bleeding at menarche” [2].

Several of the comments made by the authors are valid, and were acknowledged and addressed as limitations in the publication. Some of these include the retrospective nature, small sample size, dosing variability, changes in regimens, window of accepted height measurements, and limited available data in charts (i.e., mid-parental height and bone age). As such, we want to emphasize that we presented a pilot study on an important topic that has not been previously addressed, and our conclusions used soft terminology so as to not overstate the implications of our findings. For instance, we describe that “this study provides additional information to the overall discussion weighing the potential benefits and risks of estrogen-containing therapies over other modalities for use in management of heavy menstrual bleeding for adolescents at menarche.” We also address the difference between statistical and clinical significance in this context. Further, we agree with the need for additional, prospective, multicenter studies and state this in the text.

Regarding treatment, we specify that “estrogen-containing therapy included daily doses of 20 mcg, 30 mcg, or 35 mcg of ethinyl estradiol as monotherapy or in a combined oral contraceptive pill.” The primary treatment modality was determined to be the therapy used for the longest duration within one year after menarche and initiated within three months of menarche. Assessing dose-dependent relationships was beyond the scope of this pilot study, which was also stated as a limitation.

Inter-group demographic variability was assessed, and there were no findings of significant differences. For average age at menarche, all the groups averaged 11 years: non-hormonal (11.95926 years), estrogen-containing (11.96875 years), progesterone-only (11.03 years). Regarding the concern that “the earlier the menarche age, the shorter the final height,” this only strengthens our point, as the estrogen group had the marginally “older” age at menarche but still resulted in the shortest final height.

Further, age-dependent relationships were assessed with linear regression separately for those age <12 years and >12 years. Standardization of the outcome of interest to near-final height was performed and used in additional regression analyses, which reproduced and reinforced the initial findings.

As stated in the article, there was insufficient data available in the collective patient charts to assess bone age and parental heights. Instead, we performed an age-standardized analysis to near-final height (explained above). This supported our results.

Since this question of using estrogen for heavy menstrual bleeding has not been previously studied, our findings provide important pilot data about the possibility of disparate effects of treatment modalities on the heights of adolescents. While there are certainly limitations to this study, we still believe this work provides valuable
information. Of course, as stated in the article, further study with a prospective trial is indeed warranted.

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### References